

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Bonnert et al.

Patent No. : 7,723,373

Issue Date : May 25, 2010

Serial No. : 10/521,325

Filed : August 15, 2005

Title : INDOLE-3-SULPHUR DERIVATIVES

Art Unit : 1626

Examiner : Shawquia Young

Conf. No. : 9186

Attn.: Certificate of Corrections Branch

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

TRANSMITTAL OF REQUEST FOR CERTIFICATE OF CORRECTION

Applicants hereby request that a Certificate of Correction be issued for the above patent in accordance with the attached request.

To the best of Applicants' knowledge and belief, some of the errors sought to be corrected appear to have been made in printing of the patent by the Patent and Trademark Office. Applicants' Amendment in Reply to Action of November 14, 2008 (filed March 13, 2009) is enclosed in support of the corrections requested at col. 37, line 50 and col. 38, line 3.

Some of the errors sought to be corrected appear to have inadvertently occurred in papers as filed by Applicants. These errors, however, (i) are of a clerical or typographical nature, or of minor character; and (ii) do not involve such changes in the patent as would constitute new matter or would require re-examination. As such, the fee in the amount of \$100 as required by 37 CFR §1.20(a) is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization.

CERTIFICATE OF MAILING BY EFS-WEB FILING

I hereby certify that this paper was filed with the Patent and Trademark Office using the EFS-WEB system on this date: December 20, 2010.

Applicant : Bonnert et al.
Patent No. : 7,723,373
Issued : May 25, 2010
Serial No. : 10/521,325
Filed : August 15, 2005
Page : 2 of 2

Attorney's Docket No.: 06275-0435US1 / 100770-1P
US/R&I

Please apply any other charges or credits to Deposit Account No. 06-1050, referencing
Attorney Docket No. 06275-0435US1 / 100770-1P US/R&I.

Respectfully submitted,

Date: December 20, 2010

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Only**UNITED STATES PATENT AND TRADEMARK OFFICE**
CERTIFICATE OF CORRECTIONPage 1 of 2

PATENT NO. :: 7,723,373

APPLICATION NO :: 10/521,325

DATED :: MAY 25, 2010

INVENTOR(S) :: ROGER BONNERT, MARK DICKINSON, RUKHSANA RASUL, HITESH SANGANEE AND
SIMON TEAGUE

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 37, line 49 (Approx.), "group,or", should read -- group, or --.

Column 37, line 50 (Approx.), "may be", should read -- are --.

Column 38, line 3, "may be", should read -- are --.

Column 38, line 13, "according", should read -- according to --.

Column 38, line 17, "3 -[(4" should read -- 3-[(4 --.

Column 38, line 67, "acid" should read -- acid; --.

Column 39, line 3, "3 -chlorophenyl", should read -- 3-chlorophenyl --.

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

Page 2 of 2

PATENT NO. : 7,723,373

APPLICATION NO : 10/521,325

DATED : MAY 25, 2010

INVENTOR(S) : ROGER BONNERT, MARK DICKINSON, RUKHSANA RASUL, HITESH SANGANEE AND
SIMON TEAGUE

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 39, line 44 (Approx.), "R¹⁷ R¹⁸" should read -- R¹⁷ or R¹⁸ --.

Column 40, line 41 (Approx.), "atoms);", should read -- atoms); or --.

Column 40, line 51, "according", should read -- according to --.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Bonnert et al. Art Unit : 1626
Serial No. : 10/521,325 Examiner : Shawquia Young
Filed : August 15, 2005 Conf. No. : 9186
Title : INDOLE-3-SULPHUR DERIVATIVES

Mail Stop Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT IN REPLY TO ACTION OF NOVEMBER 14, 2008

Please amend the above-identified application as follows:

Applicant : Bonnert et al.
Serial No. : 10/521,325
Filed : August 15, 2005
Page : 2 of 14

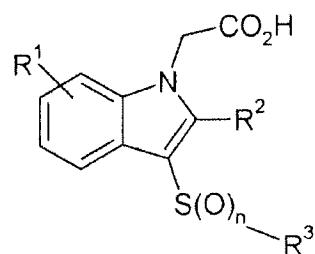
Attorney's Docket No.: 06275-435US1 / 100770-1P US

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

in which:

n represents 1 or 2;

R¹ is one or more substituents independently selected from halogen, CN, nitro, SO₂R⁴, OR⁴, SR⁴, SOR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NR⁹SO₂R⁴, NR⁹CO₂R⁴, NR⁹COR⁴, aryl, C₂-C₆ alkenyl, C₂-C₆ alkynyl or C₁₋₆alkyl, the latter five groups being optionally substituted by one or more substituents independently selected from halogen, OR⁷ and NR⁸R⁹, NR⁸R⁹, S(O)_xR⁷ where x is 0, 1 or 2;

R² is hydrogen, halogen, CN, SO₂R⁴ or CONR⁵R⁶, COR⁴ or C₁₋₇alkyl, the latter group being optionally substituted by one or more substituents independently selected from halogen atoms, OR⁸ and NR⁵R⁶, S(O)_xR⁷ where x is 0, 1 or 2;

R³ is aryl or a 5-6 membered aromatic ring containing one or more heteroatoms selected from N, S and O, each of which is optionally substituted by one or more substituents independently selected from halogen, CN, nitro, SO₂R⁴, OH, OR⁴, SR⁴, SOR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NR⁹SO₂R⁴, NR⁹CO₂R⁴, NR⁹COR⁴, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkyl, the latter three groups being optionally substituted by one or more substituents independently selected from halogen atoms, OR⁷ and NR⁸R⁹, S(O)_xR⁷ where x is 0,1 or 2;

R⁴ represents aryl, heteroaryl, or C₁-C₆ alkyl, all of which are may be optionally substituted by one or more substituents independently selected from halogen atoms, aryl, heteroaryl, OR¹⁰ and NR¹¹R¹² S(O)_xR¹³ (where x = 0, 1 or 2), CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, CN, nitro;

R⁵ and R⁶ independently represent a hydrogen atom, a C₁-C₆ alkyl group, or an aryl group, the latter two of which are may be optionally substituted by one or more substituents independently selected from halogen atoms, aryl, OR¹³ and NR¹⁴R¹⁵, CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, CN, nitro;

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached can form a 3-8 membered saturated heterocyclic ring optionally containing one or more atoms selected from O, S(O)_x where x is 0, 1 or 2, NR¹⁶, and the ring itself is optionally substituted by C₁-C₃ alkyl;

R⁷ and R¹³ independently represent a C₁-C₆ alkyl group, or an aryl or group all of which are may be optionally substituted by halogen atoms;

R⁸ represents a hydrogen atom, C(O)R⁹, C₁-C₆ alkyl (optionally substituted by halogen atoms, or an aryl group, which may also is be optionally substituted by one or more fluorine atoms); or an aryl group, which is may be optionally substituted by one or more halogen atoms;

each of R⁹, R¹⁰, R¹¹, R¹², R¹⁴, R¹⁵, independently represents a hydrogen atom, C₁-C₆ alkyl, or an aryl group (all of which are may be optionally substituted by one or more halogen atoms); and

R¹⁶ is hydrogen, C₁-₄ alkyl, -C(O)C₁-C₄ alkyl, C(O)YC₁-C₄alkyl, Y is O or NR⁷.

~~or a pharmaceutically acceptable salt or solvate thereof.~~

2. (Original) A compound according to claim 1 in which n is 2.
3. (Previously presented) A compound according to claim 1 in which R¹ is halogen, nitrile, C₁₋₆alkyl or SO₂R⁴, NO₂, NR⁹COR⁴, NR⁹SO₂R⁴, aryl, NR⁵R⁶.
4. (Previously presented) A compound according to claim 1 in which the R¹ substituent(s) is/are in the 4- and/or 5- position.
5. (Previously presented) A compound according to claim 1 in which R² is C₁₋₆alkyl.
6. (Original) A compound according to claim 4 in which R³ is phenyl substituted by halogen.
7. (Currently Amended) A compound according to claim 1 selected from:
3-[(4-chlorophenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;
5-chloro-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid;
6-chloro-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid;
7-chloro-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid;
5-chloro-3-[(4-chlorophenyl)sulfonyl]-4-cyano-2-methyl-1*H*-indole-1-acetic acid;
5-chloro-3-[(4-chlorophenyl)sulfonyl]-6-cyano-2-methyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-2,5-dimethyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-4-(ethylsulfonyl)-7-methoxy-2-methyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-5-cyano-2-methyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-5-cyano-2-methyl-1*H*-indole-1-acetic acid;
5-chloro-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid,
4-chloro-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid;
3-[(4-methoxyphenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;
3-[(3-methoxyphenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;

3-[(2-Chlorophenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;
3-[(3-Chlorophenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;
3-[(4-Cyanophenyl)sulfonyl]-2,5-dimethyl-1*H*-indole-1-acetic acid;
3-[(2-methylphenyl)sulfonyl]-2,5-Dimethyl-1*H*-indol-1-acetic acid;
3-[(2-ethylphenyl)sulfonyl]-2,5-dimethyl-1*H*-indol-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-2-methyl-4-nitro-1*H*-indole-1-acetic acid;
4-(Acetylamino)-3-[(4-chlorophenyl)sulfonyl]-2-methyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-2-methyl-4-[(methylsulfonyl)amino]- 1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-4-(ethylamino)-2-methyl-1*H*-indole-1-acetic acid;
3-[(2,6-Dichlorophenyl)sulfonyl]-2,5-dimethyl-1*H*-indole-1-acetic acid;
3-[(4-chlorophenyl)sulfonyl]-2-methyl-4-phenyl-1*H*-indole-1-acetic acid
3-[(4-chlorophenyl)sulfonyl]-5-fluoro-2-methyl-1*H*-indole-1-acetic acid,
3-[(3-chlorophenyl)sulfonyl]-5-fluoro-2-methyl- 1*H*-indole-1-acetic acid, and
5-fluoro-2-methyl-3-[[4-(trifluoromethyl)phenyl]sulfonyl]- 1*H*-indole-1-acetic acid,
or a and pharmaceutically acceptable salt salts thereof.

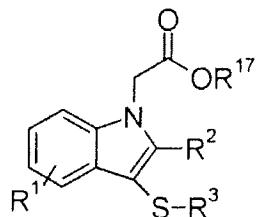
8-9. (Cancelled)

10. (Previously presented) A method of treating asthma or rhinitis, the method comprising administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt as defined in claim 1.

11-13. (Cancelled)

14. (Previously Presented) A process for the preparation of a compound of formula (I) of claim 1 which comprises:

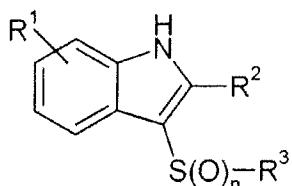
(a) oxidation of a compound of formula (II):



(II)

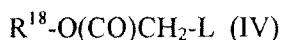
in which R¹⁷ is hydrogen or alkyl and R¹, R² and R³ are as defined in claim 1, or

(b) reaction of a compound of formula (III):



(III)

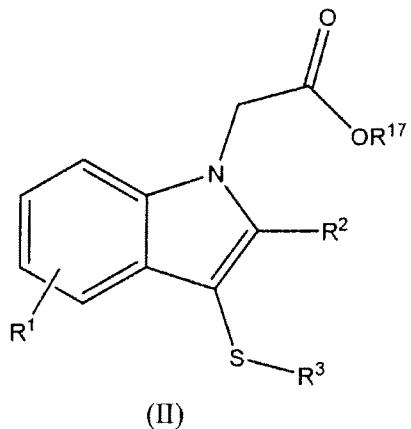
in which R¹, R² and R³ are as defined in claim 1, with a compound of formula (IV):



where R¹⁸ is an alkyl group and L is a leaving group in the presence of a base, and optionally thereafter (a) or (b) in any order:

- hydrolysing the ester group R¹⁷ or R¹⁸ to the corresponding acid
- removing any protecting group
- forming a pharmaceutically acceptable salt.

15. (Currently Amended) A compound of formula (II) or a pharmaceutically acceptable salt thereof:



wherein:

R¹⁷ is hydrogen or alkyl;

R¹ is one or more substituents independently selected from halogen, CN, nitro, SO₂R⁴, OR⁴, SR⁴, SOR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NR⁹SO₂R⁴, NR⁹CO₂R⁴, NR⁹COR⁴, aryl, C₂-C₆ alkenyl, C₂-C₆ alkynyl or C₁-alkyl, the latter five groups being optionally substituted by one or more substituents independently selected from halogen, OR⁷ and NR⁸R⁹, NR⁸R⁹, S(O)_xR⁷ where x is 0, 1 or 2;

R² is hydrogen, halogen, CN, SO₂R⁴ or CONR⁵R⁶, COR⁴ or C₁-alkyl, the latter group being optionally substituted by one or more substituents independently selected from halogen atoms, OR⁸ and NR⁵R⁶, S(O)_xR⁷ where x is 0, 1 or 2;

R³ is aryl or a 5-6 membered aromatic ring containing one or more heteroatoms selected from N, S and O, each of which is optionally substituted by one or more substituents independently selected from halogen, CN, nitro, SO₂R⁴, OH, OR⁴, SR⁴, SOR⁴, SO₂NR⁵R⁶, CONR⁵R⁶, NR⁵R⁶, NR⁹SO₂R⁴, NR⁹CO₂R⁴, NR⁹COR⁴, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkyl, the latter three groups being optionally substituted by one or more substituents independently selected from halogen atoms, OR⁷ and NR⁸R⁹, S(O)_xR⁷ where x is 0, 1 or 2;

R⁴ represents aryl, heteroaryl, or C₁-C₆ alkyl, all of which are may be optionally substituted by one or more substituents independently selected from halogen atoms, aryl, heteroaryl, OR¹⁰ and NR¹¹R¹²S(O)_xR¹³ (where x = 0, 1 or 2), CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, CN, nitro;

R⁵ and R⁶ independently represent a hydrogen atom, a C₁-C₆ alkyl group, or an aryl group, the latter two of which are may be optionally substituted by one or more substituents independently selected from halogen atoms, aryl, OR¹³ and NR¹⁴R¹⁵, CONR¹⁴R¹⁵, NR¹⁴COR¹⁵, SO₂NR¹⁴R¹⁵, NR¹⁴SO₂R¹⁵, CN, nitro;

or

R⁵ and R⁶ together with the nitrogen atom to which they are attached can form a 3-8 membered saturated heterocyclic ring optionally containing one or more atoms selected from O, S(O)_x where x is 0, 1 or 2, NR¹⁶, and the ring itself optionally substituted by C₁-C₃ alkyl;

R⁷ and R¹³ independently represent a C₁-C₆ alkyl group, or an aryl or group all of which are may be optionally substituted by halogen atoms;

R⁸ represents a hydrogen atom, C(O)R⁹, C₁-C₆ alkyl (optionally substituted by halogen atoms, or an aryl group, which is may also be optionally substituted by one or more fluorine atoms); or an aryl group, which is may be optionally substituted by one or more halogen atoms;

each of R⁹, R¹⁰, R¹¹, R¹², R¹⁴, R¹⁵, independently represents a hydrogen atom, C₁-C₆ alkyl, or an aryl group (all of which are may be optionally substituted by one or more halogen atoms); and

R¹⁶ is hydrogen, C₁-₄ alkyl, -C(O)C₁-C₄ alkyl, C(O)YC₁-C₄alkyl, Y is O or NR⁷.

Applicant : Bonnert et al.
Serial No. : 10/521,325
Filed : August 15, 2005
Page : 9 of 14

Attorney's Docket No.: 06275-435US1 / 100770-1P US

REMARKS

Claims 1-7, 10, 14, and 15 are pending in the application.

Applicants have replaced each occurrence of "may be" in claims 1 and 15 with either "is" or "are." Applicants have deleted "or a pharmaceutically acceptable salt thereof" in claim 15. No new matter is introduced by these amendments.

Rejection under 35 U.S.C. § 103

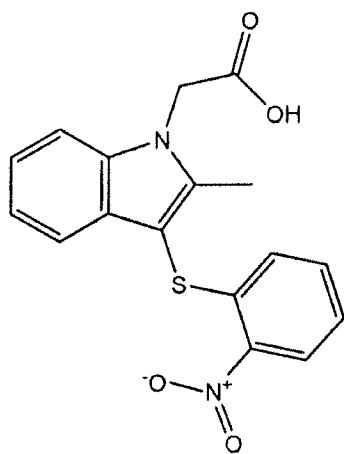
Claim 15 is rejected under 35 U.S.C. § 103 as being unpatentable over "*Luescher, et al.* (See RN 86704-63-04, CAPLUS)" (Office Action, page 3).

[1] It is Applicants' understanding, based on the abstract attached to the Office Action, that "*Luescher, et al.*" refers to the following journal article:

Lüscher, I.F. and Schneider, C.H. "51. Deblocking of *o*-Nitrophenylsulfenyl-Protected Peptides by Ammonium Thiocyanate and (2-Methyl-1-indolyl)acetic acid" *Helv. Chim. Acta.* **1983, 66, 602-605 ("Lüscher").**

A copy of the above-mentioned journal article is included with this Reply. For purposes of clarification, reference to "Lüscher" in the discussion below refers to the above-mentioned journal article and not the abstract attached to the Office Action.

[2] The Office appears to rely on the disclosure of “(2-methyl-3-(2-nitrophenylthio)-1-indolyl) acetic acid” in Lüscher as the basis for the rejection (see pages 3-5 of the Office Action). For ease of exposition, the aforementioned compound is referred to in the discussion below as “the Lüscher compound.” The chemical structure of the Lüscher compound is shown below:



According to the Office (Office Action, pages 4-5, emphasis added):

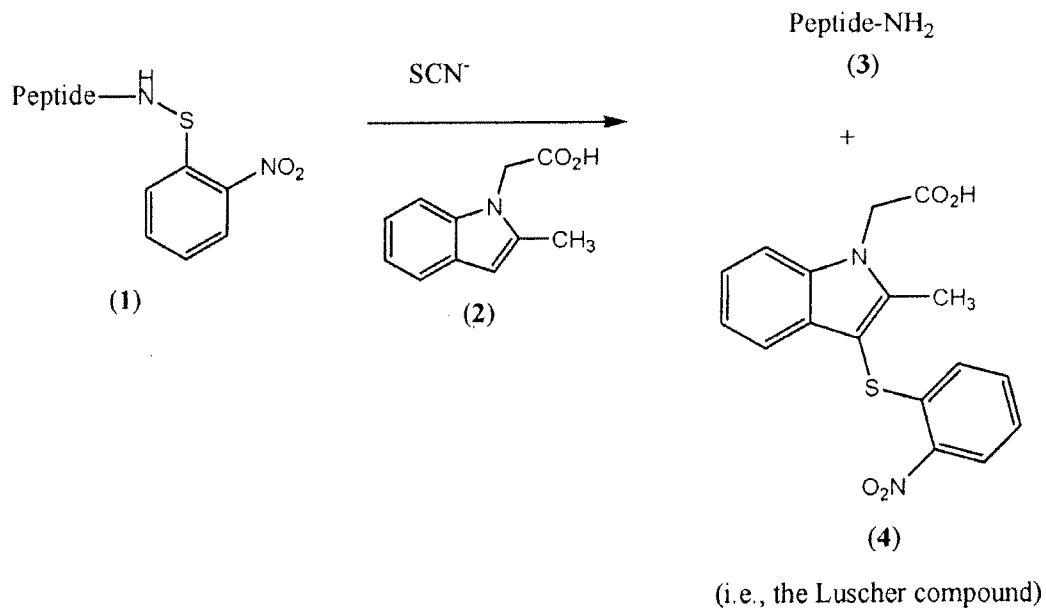
[I]t is obvious to prepare an indole derivative wherein the benzene ring is unsubstituted by an alkyl (i.e. methyl) when the art teaches a similar compound wherein the benzene ring is unsubstituted with a reasonable expectation of success. Specifically, adding a methyl substituent to the benzene ring with the same core structure as taught in the prior art is obvious absent unexpected results. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare adjacent homologs based on the teachings of the preferred embodiments in the prior art. A strong *prima facie* obviousness has been established.

This is respectfully traversed.

[3] Lüscher

Lüscher is concerned exclusively with procedures for deblocking *o*-nitrophenylsulfenyl (referred to in the discussion below by the acronym "Nps")-protected peptides. In particular, Lüscher discloses a deblocking procedure that includes exposing an Nps-protected peptide (compound (1) in Scheme 1 below) to thiocyanate ion (i.e., SCN⁻) and (2-methyl-1-indolyl) acetic acid (compound (2) in Scheme 1 below) or a salt of compound (2).

Scheme 1



In addition to providing the desired deprotected peptide (3), the Lüscher deblocking procedure described above also generates a by-product (4). As indicated in Scheme 1, this reaction by-product (4) is **the Lüscher compound**. Thus, the Lüscher compound, which is the same compound relied upon by the Office in the present rejection, is a by-product that is formed in this peptide deprotection reaction. Thus, the Lüscher compound is effectively a contaminant that must be removed in order to obtain the desired deprotected peptide in purified form.

Lüscher does not disclose any apparent utility for the Lüscher compound. Apart from the brief experimental section of Lüscher, the only other mention of the Lüscher compound in the reference concerns the facility with which the Lüscher compound can be extracted into “organic solvents” and “aqueous base” (see Lüscher at page 603 at the paragraph immediately following Table 1 and its accompanying footnotes). Finally, there is no indication that Lüscher does anything at all (much less anything useful) with the Lüscher compound once it is removed from the crude deblocking product mixture *via* extraction (see Lüscher at e.g., page 602 in the “Summary” and the experimental section on pages 604 and 605).

[4] The Federal Circuit in *Eisai Co. Ltd. v. Dr. Reddy's Laboratories, Ltd.* 533 F.3d 1353, 1358 (2008) discussed the requirements for establishing whether a claimed compound is *prima facie* obvious over a reference compound (emphasis added):

The Supreme Court's analysis in *KSR* thus relies on several assumptions about the prior art landscape. First, *KSR* assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, *KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound. See *Takeda*, 492 F.3d at 1357 (“Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound”). Third, the Supreme Court's analysis in *KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a “finite number of identified, predictable solutions,” 127 S.Ct. at 1742. In *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, 520 F.3d 1358, 1364 (Fed.Cir.2008), this court further explained that this “easily traversed, small and finite number of alternatives ... might support an inference of obviousness.” To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these “identified, predictable solutions” may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

In other words, post- *KSR*, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound.

[5] Applicants submit that the teachings of Lüscher would not have led one to select the Lüscher compound (or any other compound in Lüscher) as a lead compound for any purpose. This is discussed in more detail below.

The Lüscher compound is nothing more than a by-product of a peptide deprotection reaction. Thus, it is effectively a contaminant that must be removed in order to obtain the desired deprotected peptide in purified form. Lüscher does not disclose any apparent utility for the Lüscher compound. Apart from the brief experimental section of Lüscher, the only other mention of the Lüscher compound in the reference concerns the facility with which the Lüscher compound can be extracted into "organic solvents" and "aqueous base" (see Lüscher at page 603 at the paragraph immediately following Table 1 and its accompanying footnotes). Finally, there is no indication that Lüscher does anything at all (much less anything useful) with the Lüscher compound once it is removed from the crude deblocking product mixture *via* extraction (see Lüscher at e.g., page 602 in the "Summary" and the experimental section on pages 604 and 605).

In view of the above, the Lüscher compound does not at all appear to fall within the purview of "preferred embodiments" as is asserted by the Office. As such, it would not have been obvious to select the Lüscher compound (or any other compound in Lüscher) as a lead compound for further study or use. Accordingly, it also would not have been obvious to a person of ordinary skill in the art to make any kind of variant of the Lüscher compound. Thus, one of ordinary skill in the art would not be motivated by Lüscher to prepare the compounds claimed in claim 15 for at least this reason.

Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

Applicant : Bonnert et al.
Serial No. : 10/521,325
Filed : August 15, 2005
Page : 14 of 14

Attorney's Docket No.: 06275-435US1 / 100770-1P US

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-7, 10, 14, and 15 are rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. The recitation of "may be optionally substituted" appears to the basis for the rejection.

Applicants respectfully disagree with the grounds for the rejection; however, to expedite prosecution, Applicants have replaced each occurrence of "may be" in claims 1 and 15 with either "is" or "are."

Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

CONCLUDING FORMALITIES

Applicants submit that all claims are in condition for allowance.

The fee in the amount of \$130 for the one month extension fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of a Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 06275-435US1 / 100770-1P US.

Respectfully submitted,

Date: March 13, 2009

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